```
   1 CCAACTGCAC CTCGGTTCTA TCGATTGAAT TCCCCGGGGA TCCTCTAGAG ATCCCTCGAC

  61 CTCGACCCAC GCGTCCGGAA CCTTTGCACG CGCACAAACT ACGGGACGA TTTCTGATTG

 121 ATTTTTGGCG CTTTCGATCC ACCCTCCTCC CTTCTCATGG GACTTTGGGG ACAAAGCGTC
   1                                   M  Q  L  M  Q  Q  S  V

 181 CCGACCGCCT CGAGCGCTCG AGCAGGGCGC TATCCAGGAG CCAGGACAGC GTCGGGAACC
   9 P  T  A  E  E  A  R  A  G  R  Y  P  G  A  R  T  A  E  Q  T

 241 AGACCATGGC TCCTGGACCC CAAGATCCTT AAGTTCGTCG TCTTCATCGT CGCGGTTCTG
  29 R  P  W  L  L  D  P  K  I  L  K  F  V  V  F  I  V  A  V  L

 301 CTGCCGGTCC GGGTTGACTC TGCCACCATC CCCCGGCAGG ACGAAGTTCC CCAGCAGACA
  49 L  P  V  R  V  D  E  A  T  I  P  R  Q  D  E  V  F  Q  Q  T

 361 GTGGCCCCAC AGCAACAGAG GCGCAGCCTC AAGGAGGAGG AGTGTCCAGC AGGATCTCAT
  69 V  A  F  Q  Q  Q  R  R  E  L  K  E  E  E  C  P  A  G  S  H

 421 AGATCAGAAT ATACTGGAGC CTGTAACCCG TGCACAGAGG GTGTGGATTA CACCATTGCT
  89 R  E  E  Y  T  G  A  C  N  P  C  T  E  G  V  D  Y  T  I  A

 481 TCCAACAATT TGCCTTCTTG CCTGCTATGT ACAGTTTGTA AATCAGGTCA AACAAATAAA
 109 S  N  N  L  P  S  C  L  L  C  T  V  C  K  S  G  Q  T  N  K

 541 AGTTCCTGTA CCACGACCAG AGACACCGTG TGTCAGTGTG AAAAAGGAAG CTTCCAGGAT
 129 S  S  C  T  T  T  R  D  T  V  C  Q  C  E  K  G  S  F  Q  D

 601 AAAAACTCCC CTGAGATGTG CCGGACGTGT AGAACAGGGT GTCCCAGAGG GATGGTCAAG
 149 K  N  S  P  E  M  C  R  T  C  R  T  G  C  P  R  G  M  V  K

 661 GTCAGTAATT GTACGCCCCG GAGTGACATC AAGTGCAAAA ATGAATCAGC TGCCAGTTCC
 169 V  S  N  C  T  P  R  S  D  I  K  C  K  N  K  S  A  A  S  S

 721 ACTGGGAAAA CCCCAGCAGC GGAGGAGACA GTGACCACCA TCCTGGGGAT GCTTGCCTCT
 189 T  G  K  T  P  A  A  K  K  T  V  T  T  I  L  G  M  L  A  S

 781 CCCTATCACT ACCTTATCAT CATAGTGGTT TTAGTCATCA TTTTAGCTGT GGTTGTGGTT
 209 P  Y  H  Y  L  I  I  I  V  V  L  V  I  I  L  A  V  V  V  V

 841 GGCTTTTCAT GTCGGAAGAA ATTCATTTCT TACCTCAAAG GCATCTGCTC AGGTGGTGGA
 229 G  F  S  C  R  K  K  F  I  S  Y  L  K  G  I  C  S  G  G  G

 901 GGAGGTCCCG AACGTGTGCA CAGAGTCCTT TTCCGGCGGC GTTCATGTCC TTCACGAGTT
 249 G  G  P  E  R  V  H  R  V  L  F  R  R  R  S  C  P  S  R  V

 961 CCTGGGGCGG AGGACAATGC CCGCAACGAG ACCCTGAGTA ACAGATACTT GCAGCCCACC
 269 P  G  A  E  D  N  A  R  N  E  T  L  S  N  R  Y  L  Q  P  T

1021 CAGGTCTCTG AGCAGGAAAT CCAAGGTCAG GAGCTGGCAG AGCTAACAGG TGTGACTGTA
 289 Q  V  S  E  Q  E  I  Q  G  Q  E  L  A  K  L  T  G  V  T  V

1081 GAGTYGCCAG AGGAGCCACA GCGTCTGCTG GAACAGGCAG AAGCTGAAGG GTGTCAGAGG
 309 E  Xaa  P  E  E  P  Q  R  L  L  K  Q  A  E  A  E  G  C  Q  R

1141 AGGAGGCTGC TGGTTCCAGT GAATGACGCT GACTCCGCTG ACATCAGCAC CTTGCTGGAT
 329 R  R  L  L  V  P  V  N  D  A  D  S  A  D  I  S  T  L  L  D

1201 GCCTCGGCAA CACTGGAAGA AGGACATGCA AAGGAAACAA TTCAGGACCA ACTGGTGGGC
 349 A  S  A  T  L  E  E  G  E  A  K  E  T  I  Q  D  Q  L  V  G

1261 TCCGAAAAGC TCTTTTATGA AGAAGATGAG GCAGGCTCTG CTACGTCCTG CCTGTGAAAG
 369 S  E  K  L  F  Y  E  E  D  E  A  G  S  A  T  S  C  L

1321 AATCTCTTCA GGAAACCAGA GCTTCCCTCA TTTACCTTTT CTCCTACAAA GGGAAGCAGC

1381 CTGGAAGAAA CAGTCCAGTA CTTGACCCAT GCCCCAACAA ACTCTACTAT CCAATATGGG

1441 GCAGCTTACC AATGGTCCTA GAACTTTGTT AACGCACTTG GAGTAATTTT TATGAAATAC

1501 TGCGTGTGAT AAGCAAACGG GAGAAATTTA TATCAGATTC TTGGCTGCAT AGTTATACGA

1561 TTGTGTATTA AGGGTCGTTT TAGGCCACAT GCGGTGGCTC ATGCCTGTAA TCCCAGCACT

1621 TTGATAGGCT GAGGCAGGTG GATTGCTTGA GCTCGGGAGT TTGAGACCAG CCTCATCAAC

1681 ACAGTGAAAC TCCATCTCAA TTTAAAAAGA AAAAAAGTGG TTTTAGGATG TCATTCTTTG

1741 CAGTTCTTCA TCATGAGACA AGTCTTTTTT TCTGCTTCTT ATATTGCAAG CTCCATCTCT

1801 ACTGGTGTGT GCATTTAATG ACATCTAACT ACAGATGCCG CACAGCCACA ATGCTTTGCC

1861 TTATAGTTTT TTAACTTTAG AACGGGATTA TCTTGTTATT ACCTGTATTT TCAGTTTCGG

1921 ATATTTTTGA CTTAATGATG AGATTATCAA GACGTACCCC TATGCTAAGT CATGAGCATA

1981 TGGACTTACG AGGGTTCGAC TTAGAGTTTT GAGCTTTAAG ATAGGATTAT TGGGGGCTTA

2041 CCCCCACCTT AATTAGAAGA AACATTTTAT ATTGCTTTAC TA
```

Fig. 1A

```
RTD      1  --MGLWGQSVPTASSARA--GRYPGARTASGTRPWLLDPKILKFVVFIVA
DR4     51  GRGALPTSMGQHGPSARARAGRAPGPRPAREASPRLRVHKTFKFV--VVG
DR5      1  --MEQRGQNAPAASGARKRHG--PGPREARGARPGLRVPKTLVLV--VVA
DcR1     1  ---------------------------------MARIPKTLKFVVVIVA

RTD     47  VLLPVRVDSATIPRQDEVPQQTVAPQQQRRSLKEEECPAGSHRSEYTGAC
DR4     99  VLLQVVPSSAATIKLH---DQSIGTQQWEHSPLGELCPPGSHRSERPGAC
DR5     45  VLLLVSAESALITQQDLAPQQRAAPQQKRSSPSEGLCPPGHHISEDGRDC
DcR1    17  VLLPVLAYSATTARQEEVPQQTVAPQQQRHSFKGEECPAGSHRSEHTGAC

                         ----------------CRD1-------------
RTD     97  NPCTEGVDYTIASNNLPSCLLCTVCKSGQTNKSSCTTTRDTVCQCEKGSF
DR4    146  NRCTEGVGYTNASNNLFACLPCTACKSDEEERSPCTTTRNTACQCKPGTF
DR5     95  ISCKYGQDYSTHWNDLLFCLRCTRCDSGEVELSPCTTTRNTVCQCEEGTF
DcR1    67  NPCTEGVDYTNASNNEPSCFPCTVCKSDQKHKSSCTMTRDTVCQCKEG

            ----------CRD2-----------
RTD    147  QDKNSPEHCRTCRTGCPRGHVKVSNCTPRSDIKCKNESAASSTGKTPAAE
DR4    196  RNDNSAEHCRKCSTGCPRGHVKVKDCTPWSDIECVHKESGNGHNIW----
DR5    145  REEDSPEHCRKCRTGCPRGHVKVGDCTPWSDIECVHKESGIIIGVTVAA-
DcR1   117  RNENSPEHCRKCSR-CPSGEVQVSNCTSWDDIQCVEEFGANAT------
```

Fig. 1B

```
RTD      233 RKKFISYLKGICSGGGGGPERVHRVLFRRRSCPSRVPGAEDNARNETLSN
DR4      269 -GGDPKCMDRVCFWRLG--------------LLRGPGAEDNAHNEILSN
DR5      209 --KVLPYLKGICSGGGGDPERVDR--------SSQRPGAEDNVLNEIVSI

RTD      283 RYLQPTQVSEQEIQGQELAELTGVTVESPEEPQRLLEQAEAEGCQRRRLL
DR4      303 ADSLSTFVSEQQMESQEPADLTGVTVQSPGEAQCLLGPAEAEGSQRRRLL
DR5      250 --LQPTQVPEQEMEVQEPAEPTGVNMLSPGESEHLLEPAEAERSQRRRLL

                                    DD
RTD      333 VPVNDAD-----------------------------------------
DR4      353 VPANGADPTETLMLFFDKFANIVPFDSWDQLMRQLDLTKNEIDVVRAGTA
DR5      298 VPANEGDPTETLRQCFDDFADLVPFDSWEPLMRKLGLMDNEIKVAKAEAA

RTD      340 ----------------SADISTLLDASATLEEGMAKETIQDQLVGSE
DR4      403 GPGDALYAMLMKWVNKTGRNASIMTLLDALERMEERMAKEKIQDLLVDSG
DR5      348 GHRDTLYTMLIKWVNKTGRDASVMTLLDALETLGERLAKQKIEDHLLSSG

RTD      371 KLFYEEDEAGSATSCL
DR4      453 KFIYLEDGTGSAVSLE
DR5      398 KFMYLEGNADSALS
```

Fig. 1C

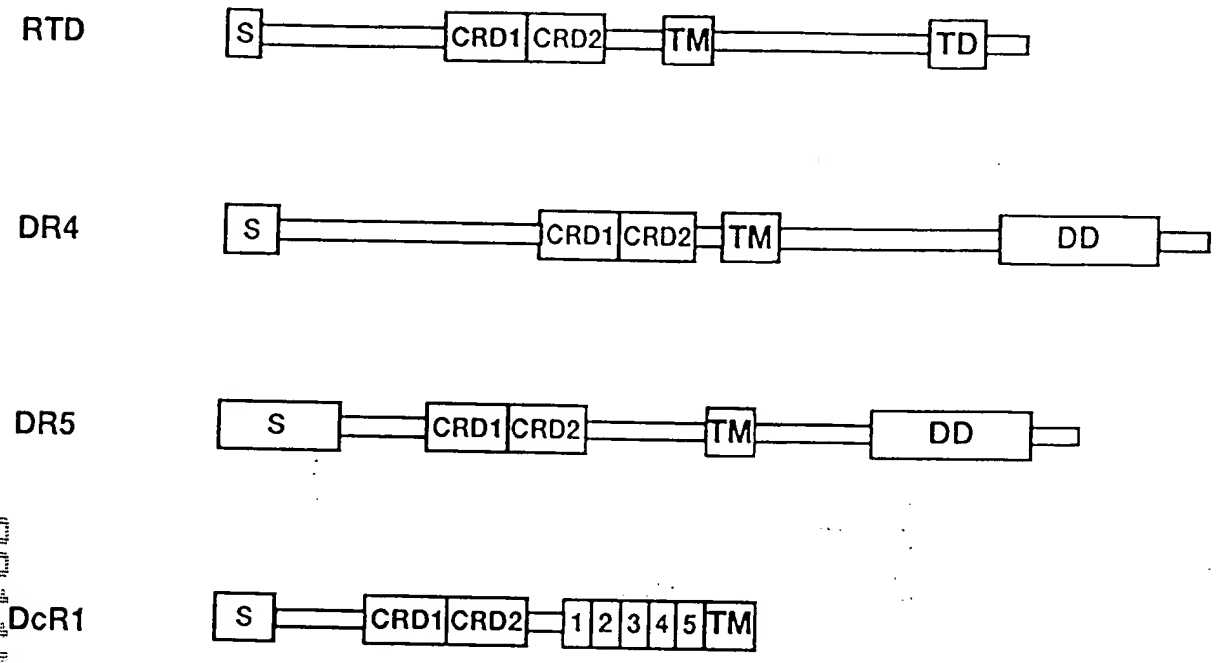
RTD
S
CRD1
CRD2
TM
TD
DR4
S
CRD1
CRD2
TM
DD
DR5
S
CRD1
CRD2
TM
DD
DcR1
S
CRD1
CRD2
1
2
3
4
5
TM

Fig. 1D

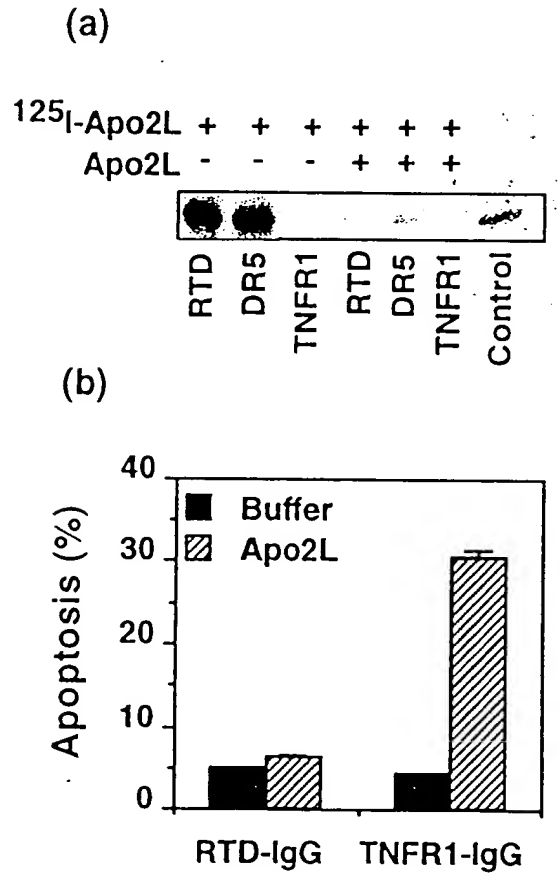
(a)
125I-Apo2L + + + + + +
Apo2L - - - + + +
RTD
DR5
TNFR1
RTD
DR5
TNFR1
Control
(b)
Apoptosis (%)
40
30
20
10
0
Buffer
Apo2L
RTD-IgG
TNFR1-IgG

Fig. 2

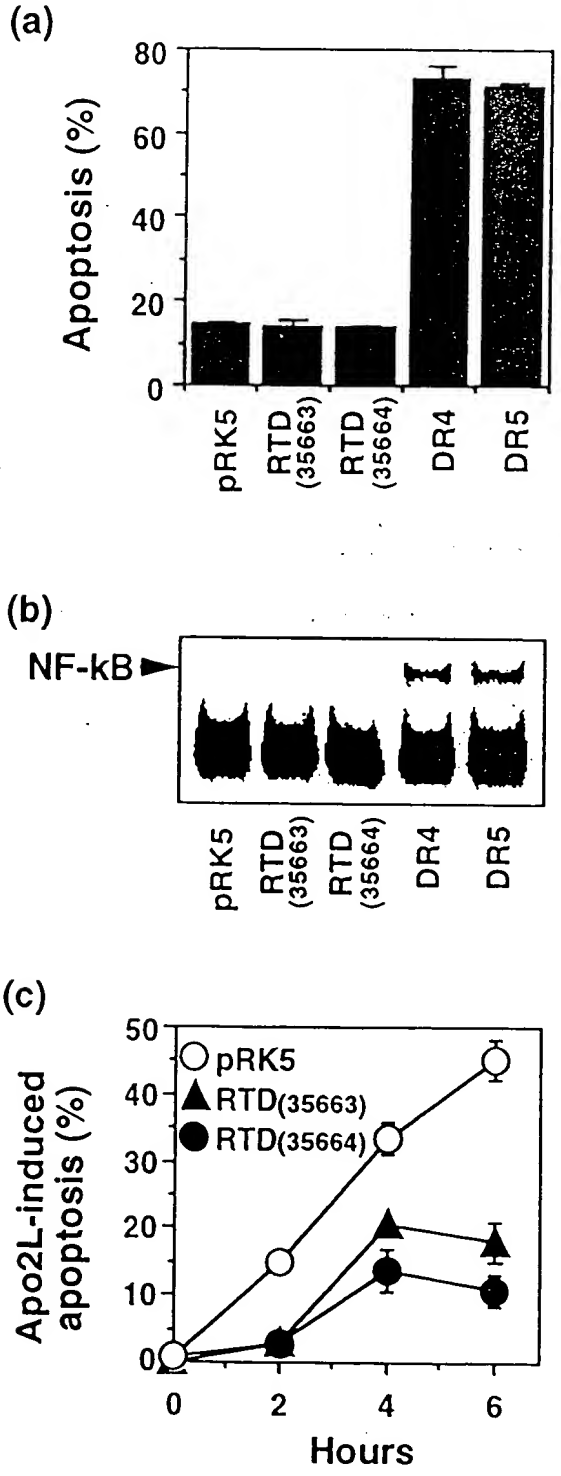
(a)
Apoptosis (%)
80
60
40
20
0
pRK5
RTD (35663)
RTD (35664)
DR4
DR5
(b)
NF-kB
pRK5
RTD (35663)
RTD (35664)
DR4
DR5
(c)
Apo2L-induced apoptosis (%)
50
40
30
20
10
0
pRK5
RTD(35663)
RTD(35664)
0
2
4
6
Hours

Fig. 3

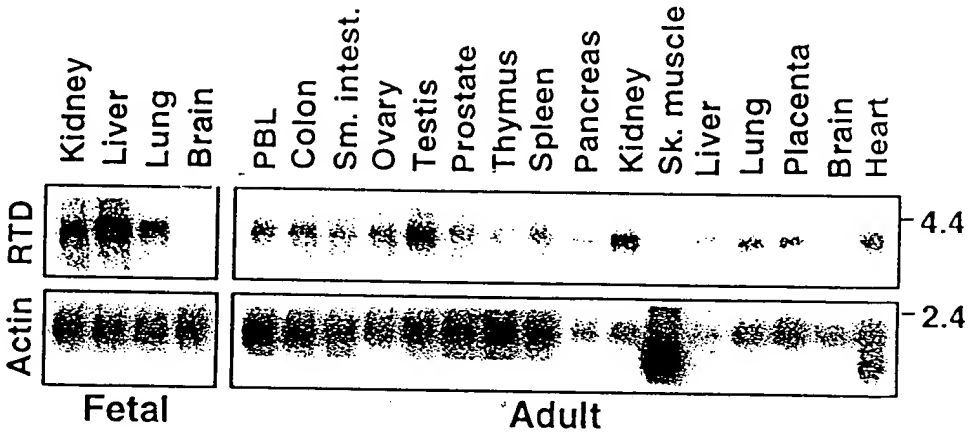
Kidney
Liver
Lung
Brain
PBL
Colon
Sm. intest.
Ovary
Testis
Prostate
Thymus
Spleen
Pancreas
Kidney
Sk. muscle
Liver
Lung
Placenta
Brain
Heart
RTD
Actin
4.4
2.4
Fetal
Adult

Fig. 4